REMARKS

Claims 1-4 and 6-11 are pending in this application. Claims 1-4 and 6 have been amended. Claim 5 has been cancelled without prejudice to or disclaimer of the subject matter contained therein.

Applicants, by canceling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Independent claim 1 has been amended to recite, "A pharmaceutical suspension formulation comprising

a. as a first active ingredient, particles of R,R-formoterol or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation,

b. as a second active ingredient, particles of ciclesonide or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation, and

c. a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof,

wherein said first active ingredient and said second active ingredient are the sole active ingredients in said pharmaceutical suspension formulation, and are readily dispersible, and upon redispersion do not flocculate as to prevent reproducing dosing of said first active ingredient and/or said second active ingredient."

Similar amendments have been made to claims 2 and 4. Support for these claims as amended can be found throughout the specification and claims as

originally filed.

Specifically, support for the limitation "active ingredient" may be found at page 4, last paragraph and page 5, first paragraph of the instant specification. Support for the limitation "R,R-formoterol" may be found in originally filed claim 5, now cancelled without prejudice. Support for the limitation "sole active ingredients" may be found in the example formulations recited on page 10 of the instant specification, wherein the sole active ingredients in the formulation are ciclesonide and formoterol. Support for the limitation "are readily dispersible, and upon redispersion do not flocculate as to prevent reproducing dosing of said first active ingredient and/or said second active ingredient" may be found at page 4, 2nd paragraph of the instant specification.

Claim 4 has further been amended to recite "further comprising a surfactant" as suggested by the Examiner.

No new matter has been added.

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. Objection to claim 4

The Examiner requests that claim 4 be amended to recite the phrase "further comprising" or "further," before the phrase "a surfactant" in claim 4.

Response

Applicants respectfully submit that claim 4 has been amended as requested by the Examiner. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw these objections.

II. Rejection of claims 1, 3-6, 9 and 11 under 35 U.S.C. §103(a) as being unpatentable over Aberg et al. (US Patent No. 5,795,564) in view of Burt (US Publication No. 2002/0030068), Garcia-Marcos et al. and Calatayud et al. (US Patent No. 5,482,934)

Claims 1, 3-6, 9 and 11 have been rejected under 35 USC § 103(a) as being unpatentable over Aberg et al. in view of Burt, Garcia-Marcos et al. ("Inhaled corticosteroids plus long-acting beta2-agonists as combined therapy in asthma," Expert Opin. Pharmacother., April 2003, 4(1), pp 23-29) ("Garcia") and Calatayud et al. Applicants note that claims 2, 7-8 and 10 were not included in this rejection.

Response

Applicants respectfully note that claim 5 has been cancelled without prejudice, rendering the basis for this rejection moot.

As to the remaining claims, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if

not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *See KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicants submit that a proper case of *prima facie* obviousness has not been established because whether taken alone, or in combination, none of Aberg et al., Burt, Garcia and/or Calatayud et al. teach or suggest every element of the presently claimed subject matter, as required by *In re Wilson*.

Amended independent claim 1 recites Independent claim 1 has been amended to recite, "A pharmaceutical suspension formulation comprising

a. as a first active ingredient, particles of R,R-formoterol or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation,

b. as a second active ingredient, particles of ciclesonide or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation and

c. a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof,

wherein said first active ingredient and said second active ingredient are the sole active ingredients in said pharmaceutical suspension formulation, and are readily dispersible, and upon redispersion do not flocculate as to prevent

reproducing dosing of said first active ingredient and/or said second active ingredient."

Conversely, Aberg et al discloses a metered dose inhaler containing a suspension formulation comprising only R,R-formoterol fumarate dihydrate as the active ingredient. As such, Aberg et al. is absolutely silent regarding the presently claimed formulation comprising particles of R,R-formoterol and ciclesonide as the sole active ingredients being readily dispersible, and upon redispersion, not flocculating as to prevent reproducing dosing of said first active ingredient and/or said second active ingredient as presently claimed.

Therefore, Aberg et al. do not "teach or suggest all the limitations of the claims" as required by *In re Wilson*. The Burt et al. reference does not remedy the deficiencies of Aberg et al. Burt et al. merely describes suitable alternative propellants include HFA-134a (1,1,1,2-tetrafluoroethane) and HFA-227 (1,1,1,2,3,3,3-heptafluoropropane) which may be combined with a combination of formoterol and an inhaled corticosteroid. As such, Burt et al. does not discuss or contemplate a pharmaceutical suspension formulation comprising particles of R,R-formoterol and ciclesonide as the sole active ingredients being readily dispersible, and upon redispersion, not flocculating as to prevent reproducing dosing of said first active ingredient and/or said second active ingredient as presently claimed.

The Garcia reference does not remedy the deficiencies of the Aberg et al. and Burt et al. references. Garcia discusses the combination of formoterol and budesonide. More specifically, Garcia discusses improved lung function when combined with both low and high doses of budesonide in comparison to administering budesonide alone. Thus, Garcia does not teach a pharmaceutical suspension formulation comprising particles of R,R-formoterol and ciclesonide as the

sole active ingredients being readily dispersible, and upon redispersion, not flocculating as to prevent reproducing dosing of said first active ingredient and/or said second active ingredient as presently claimed.

The Calatayud et al. reference does not remedy the deficiencies of the aforementioned references since it does not discuss anywhere the use of R,R-formoterol in conjunction with ciclesonide as presently claimed.

Therefore, the cited references do not establish a *prima facie* case of obviousness against the presently claimed subject matter for at least the reason that the cited references do not teach each and every element of the presently pending claims as required by *In re Wilson*.

Without such a teaching contained in the references, the Examiner cannot "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements" in such a way as to arrive at the presently claimed subject matter with a reasonable expectation of success as required by *KSR* and *Amgen*, supra.

As such, Applicants respectfully request that the Examiner reconsider and withdraw this rejection against the presently pending claims.

III. Rejection of claims 2 and 7-8 under 35 U.S.C. §103(a) as being unpatentable over Aberg et al. in view of Burt, Garcia-Marcos et al. and Calatayud et al., and further in view of Fassberg et al. (US Patent No. 5,474,759)

Claims 2 and 7-8 have been rejected under 35 USC § 103(a) as being unpatentable over Aberg et al. in view of Burt, Garcia-Marcos et al. and Calatayud et al. in view of Fassberg et al. (US 5,474,759).

Response

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section II. Also, all references other than the Fassberg et al. reference are discussed in detail in Section II. For the sake of brevity, the discussion of the relevant authority and all references other than the Fassberg et al. reference are incorporated herein in their entirety.

The Examiner asserts that Fassberg et al. teaches pharmaceutical aerosol formulations comprising a medicament, a surfactant, an excipient and a propellant and thus, renders obvious claims 2 and 7-8 which specifically recite a surfactant. Thus, the Examiner relies on Fassberg et al. for its alleged disclosure of surfactants and excipients.

Applicants respectfully note, however, that there is nothing contained in the Fassberg et al. reference that remedies the deficient teachings of the Aberg et al., Burt, Garcia-Marcos et al. and Calatayud et al. references. The rejected claims are free of the prior art for the reasons discussed above (see, Section II) and Applicants' arguments stated above are incorporated herein by reference in their entirety.

Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established for at least the reasons set forth above in Section II. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

IV. Rejection of claims 1, 3, 5, 9 and 11 under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al.

Claims 1, 3, 5, 9 and 11 have been rejected under 35 USC § 103(a) as being unpatentable over Gavin in view of Calatayud et al.

Response

Applicants respectfully note that claim 5 has been cancelled without prejudice, rendering the basis for this rejection moot.

As to the remaining claims, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section II. Also, the Calatayud et al. reference is discussed in detail in Section II. For the sake of brevity, the discussion of the relevant authority and the Calatayud et al. reference is incorporated herein in its entirety.

The Examiner asserts that Gavin et al. teaches medicinal compositions comprising (R,R)-formoterol and rofleponide as well as a propellant such as 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane or mixtures thereof. Thus, the Examiner relies on Gavin et al. for its alleged disclosure of formoterol with rofleponide, a corticosteroid.

Applicants respectfully note, however, that the Gavin reference requires an active ingredient other than those presently claimed. In particular, the presently pending claims recite that "the sole active ingredients" are "particles of R,R-formoterol or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation," and "particles of ciclesonide or a pharmaceutically acceptable salt thereof, said particles being suspended in the formulation".

As such, Gavin's disclosure cannot render the presently claimed subject matter obvious because it does not teach "[a]" pharmaceutical suspension formulation comprising" only the specific active ingredients of the presently claimed subject matter. Instead, Gavin requires the presence of the active ingredient rofleponide.

Accordingly, Gavin does not teach each and every element of the presently

pending claims as required by *In re Wilson* and Applicants therefore respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

V. Rejection of claims 2, 4 and 7-8 under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al. and further in view of Fassberg et al.

Claims 2, 4, 7 and 8 have been rejected under 35 USC § 103(a) as being unpatentable over Gavin in view of Calatayud et al. and further in view of Fassberg et al.

Response

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section II. Also, all cited references have been discussed in detail in previous sections. For the sake of brevity, the discussion of the relevant authority and all references are incorporated herein in their entirety.

The rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety. Namely, the primary Gavin reference requires the presence of an active ingredient other than those specifically recited in the presently pending claims. In particular, Gavin requires the presence of the active ingredient "rofleponide" in his pharmaceutical formulation. As such, Gavin's disclosure cannot render the presently claimed subject matter obvious because it does not teach "[a]" pharmaceutical suspension formulation comprising" only the specific active ingredients of the presently claimed subject matter.

Accordingly, Gavin does not teach each and every element of the presently pending claims as required by *In re Wilson* and Applicants therefore respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

VI. Rejection of claims 2, 4 and 7-8 under 35 U.S.C. §103(a) as being unpatentable over Gavin et al. (WO 01/78738) in view of Calatayud et al. and further in view of Keller et al. (WO 00/07567)

Claims 2, 4, 7 and 8 have been rejected under 35 USC § 103(a) as being unpatentable over Gavin in view of Calatayud et al. and further in view of Keller et al.

Response

In view of the following, this rejection is respectfully traversed.

A brief outline of relevant authority is set forth above in Section II. Also, all references other than the Keller et al. reference are discussed in detail in Sections II and IV. For the sake of brevity, the discussion of the relevant authority and all references other than the Keller et al. reference is incorporated herein in their entirety.

The Examiner asserts that Keller et al. teaches that the inclusion of solid salts of cromoglycic acid and/or nedocromil as a vehicle at non-therapeutically or non-prophylactically effective concentrations improves the dispersion characteristics and the chemical and physical stability or active ingredients which are sensitive to moisture and are present in pharmaceutical aerosol suspension formulations.

Thus, the Examiner relies on Keller et al. for its alleged disclosure that the inclusion of disodium cromoglycate or nedocromil sodium to formulations can be used to stabilize moisture-sensitive compounds, such as formoterol fumarate as well as to reduce the tendency to adhesion of electrostatically charged active

compounds, such as micronized corticosteroids.

The rejected claims are free of the prior art for the reasons discussed above (see, Section IV) and Applicants' arguments stated above are incorporated herein by reference in their entirety. Namely, the primary Gavin reference requires the presence of an active ingredient other than those specifically recited in the presently pending claims. In particular, Gavin requires the presence of the active ingredient "rofleponide" in his pharmaceutical formulation. As such, Gavin's disclosure cannot render the presently claimed subject matter obvious because it does not teach "[a]" pharmaceutical suspension formulation comprising" only the specific active ingredients of the presently claimed subject matter.

Accordingly, Gavin does not teach each and every element of the presently pending claims as required by *In re Wilson* and Applicants therefore respectfully submit that a *prima facie* case of obviousness has not been established. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection.

VII. Provisional rejection of claims 1 and 5 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent Application No. 10/537,356 in view of Burt and Aberg et al.

In this provisional rejection of claims 1 and 5, the Examiner asserts that independent claim 6 of copending '356 application claims a formulation comprising R,R-formoterol and ciclesonide in a form administrable from a dry powder inhaler.

Applicants respectfully submit that, upon an indication that the claims are otherwise allowable, applicants will either address this provisional rejection or file a terminal disclaimer.

CONCLUSION

In view of the foregoing, applicants respectfully submit that the presently pending claims are patentable over the cited references. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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